

Mindin and spondin proteins are secreted proteins that are structurally related to one another and which have been identified in a variety of organisms. For example, Higashijima et al., Dev Biol. 192:211-227 (1997) have reported the identification of spondin and mindin expression in floor plate cells in the zebrafish embryonic axis, thereby suggesting that mindin and spondin proteins play important roles in embryonic development. This same group has reported that mindin and spondin proteins function as extracellular matrix proteins that have a high affinity for the basal lamina. (Id.). It has been reported that F-spondin is a secreted protein that promotes neural adhesion and neurite extension (Klar et al., Cell 69:95-110 (1992) and that M-spondin is an extracellular matrix protein that localizes to muscle attachment sites in Drosophila (Umemiya et al., Dev. Biol. 186:165-176 (1997)). Thus, there is significant interest in identifying novel polypeptides having homology to the mindin and spondin proteins. We herein describe the identification and characterization of a novel polypeptide having homology to mindin2 and mindin1, designated herein as PRO866.

38. PRO871

Cyclophilins are a family of proteins that bind to cyclosporin A and possess peptidyl-prolyl cis-trans isomerase activity (Sherry et al., Proc. Natl. Acad. Sci. USA 95:1758-1763 (1998)). In addition, cyclophilins are secreted by activated cells and act in a cytokine-like manner, presumably via signaling through a cell surface cyclophilin receptor. Host cell-derived cyclophilin A has been shown to be incorporated into HIV-1 virions and its incorporation has been shown to be essential for viral infectivity. Thus, one or more of the cyclophilins may be directly associated with HIV-1 infectivity. Given the obvious importance of the cyclophilin proteins, there is substantial interest in identifying novel polypeptides which have sequence homology to one or more of the cyclophilin proteins. We herein describe the identification and characterization of a novel polypeptide having homology to cyclophilin-like protein CyP-60, designated herein as PRO871.

39. PRO873

Enzymatic proteins play important roles in the chemical reactions involved in the digestion of foods, the biosynthesis of macromolecules, the controlled release and utilization of chemical energy, and other processes necessary to sustain life. Enzymes have also been shown to play important roles in combating various diseases and disorders. For example, liver carboxylesterases have been reported to assist in sensitizing human tumor cells to the cancer prodrugs. Danks et al., report that stable expression of the cDNA encoding a carboxylesterase in Rh30 human rhabdomyosarcoma cells increased the sensitivity of the cells to the CPT-11 cancer prodrug 8.1-fold. Cancer Res. (1998) 58(1):20-22. The authors propose that this prodrug/enzyme combination could be exploited therapeutically in a manner analogous to approaches currently under investigation with the combinations of ganciclovir/herpes simplex virus thymidine kinase and 5-fluorocytosine/cytosine deaminase. van Pelt et al. demonstrated that a 55 kD human liver carboxylesterase inhibits the invasion of Plasmodium falciparum malaria sporozoites into primary human hepatocytes in culture. J Hepatol (1997) 27(4):688-698.

Carboxylesterases have also been found to be of importance in the detoxification of drugs, pesticides and other xenobiotics. Purified human liver carboxylesterases have been shown to be involved in the metabolism of various drugs including cocaine and heroin. Prindel et al. describe the purification and cloning of a broad substrate specificity human liver carboxylesterase which catalyzes the hydrolysis of cocaine and heroin and which

may play an important role in the degradation of these drugs in human tissues. J. Biol. Chem. (1997) 6:272(23):14769-14775. Brzenzinski *et al.* describe a spectrophotometric competitive inhibition assay used to identify drug or environmental esters that are metabolized by carboxylesterases. Drug Metab Dispos (1997) 25(9):1089-1096.

In light of the important physiological roles played by carboxylesterases, efforts are being undertaken by both industry and academia to identify new, native carboxylesterase homologs. We herein describe the identification and characterization of a novel polypeptide having homology to carboxylesterase, designated herein as PRO873.

40. PRO940

CD33 is a cell-surface protein that is a member of the sialoadhesin family of proteins that are capable of mediating sialic-acid dependent binding with distinct specificities for both the type of sialic acid and its linkage to subterminal sugars. CD33 is specifically expressed in early myeloid and some monocyte cell lineages and has been shown to be strongly associated with various myeloid tumors including, for example, acute non-lymphocytic leukemia (ANLL). As such, CD33 has been suggested as a potential target for the treatment of cancers associated with high level expression of the protein. There is, therefore, significant interest in the identification of novel polypeptides having homology to CD33. In fact, one CD33 homolog (designated CD33L) has already been identified and described (see Takei *et al.*, Cytogenet. Cell Genet. 78:295-300 (1997)). We herein describe the identification of another novel polypeptide having homology to CD33, designated herein as PRO940. The novel polypeptide described herein also exhibits significant homology to the human OB binding proteins designated HSU71382_1 and HSU71383_1 in the Dayhoff database (version 35.45 SwissProt 35).

41. PRO941

Cadherins are a large family of transmembrane proteins. Cadherins comprise a family of calcium-dependent glycoproteins that function in mediating cell-cell adhesion in virtually all solid tissues of multicellular organisms. At least cadherins 1-13 as well as types B, E, EP, M, N, P and R have been identified and characterized. Among the functions cadherins are known for, with some exceptions, are that cadherins participate in cell aggregation and are associated with cell-cell adhesion sites. Recently, it has been reported that while all cadherins share multiple repeats of a cadherin specific motif believed to correspond to folding of extracellular domains, members of the cadherin superfamily have divergent structures and, possibly, functions. In particular it has been reported that members of the cadherin superfamily are involved in signal transduction. See, Suzuki, J. Cell Biochem., 61(4):531-542 (1996). Cadherins are further described in Tanihara *et al.*, J. Cell Sci., 107(6):1697-1704 (1994), Aberle *et al.*, J. Cell Biochem., 61(4):514-523 (1996) and Tanihara *et al.*, Cell Adhes. Commun., 2(1):15-26 (1994). We herein describe the identification and characterization of a novel polypeptide having homology to a cadherin protein, designated herein as PRO941.

42. PRO944

Clostridium perfringens enterotoxin (CPE) is considered to be the virulence factor responsible for causing the symptoms of *C. perfringens* type A food poisoning and may also be involved in other human and

veterinary illnesses (McClane, *Toxicon*. 34:1335-1343 (1996)). CPE carries out its adverse cellular functions by binding to an approximately 50 kD cell surface receptor protein designated the Clostridium perfringens enterotoxin receptor (CPE-R) to form an approximately 90,000 kD complex on the surface of the cell. cDNAs encoding the CPE-R protein have been identified characterized in both human and mouse (Katahira et al., *J. Cell Biol.* 136:1239-1247 (1997) and Katahira et al., *J. Biol. Chem.* 272:26652-26658 (1997)). Since the CPE toxin has been reported to cause a variety of illnesses in mammalian hosts and those illnesses are initiated by binding of the CPE toxin to the CPE-R, there is significant interest in identifying novel CPE-R homologs. We herein describe the identification and characterization of a novel polypeptide having homology to the CPE-R, designated herein as PRO944.

43. PRO983

Membrane-bound proteins include not only cell-surface membrane-bound proteins, but also proteins that are found on the surface of intracellular vesicles. These vesicles are involved in exocytosis, which is the fusion of secretory vesicles with the cellular plasma membrane, and have two main functions. One is the discharge of the vesicle contents into the extracellular space, and the second is the incorporation of new proteins and lipids into the plasma membrane itself. Exocytosis can be either constitutive or regulated. All eukaryotic cells exhibit constitutive exocytosis, which is marked by the immediate fusion of the secretory vesicle after formation. In contrast, regulated exocytosis results in the accumulation of the secretory vesicles that fuse with the plasma membrane upon receipt of an appropriate signal by vesicle-associated membrane proteins. Usually, this signal is an increase in the cytosolic free Ca^{2+} concentration. However, regulated exocytosis that is independent of Ca^{2+} has been reported (see, e.g. Fujita-Yoshigaki *et al. J. Biol. Chem.* (1996) 31:271(22):13130-13134). Regulated exocytosis is crucial to many specialized cells, including neurons (neurotransmitter release from synaptic vesicles), adrenal chromaffin cells (adrenaline secretion), pancreatic acinar cells (digestive enzyme secretion), pancreatic β -cells (insulin secretion), mast cells (histamine secretion), mammary cells (milk protein secretion), sperm (enzyme secretion), egg cells (creation of fertilization envelope) and adipocytes (insertion of glucose transporters into the plasma membrane).

Disorders involving exocytosis are known. For example, inflammatory mediator release from mast cells leads to a variety of disorders, including asthma. Similarly, Chediak-Higashi Syndrome (CHS) is a rare autosomal recessive disease in which neutrophils, monocytes and lymphocytes contain giant cytoplasmic granules. Accordingly, the proteins involved in exocytosis are of paramount interest and efforts are being undertaken by both industry and academia to identify new, vesicle-associated proteins. For example, Skehel *et al.* identified a 33-kilodalton membrane protein in Aplysia, termed VAP-33, which is required for the exocytosis of neurotransmitter. *Science* (1995) 15:269(5230):1580-1583, and *Neuropharmacology* (1995) 34(11):1379-1385. Many efforts are focused on the screening of mammalian recombinant DNA libraries to identify the coding sequences for novel vesicle-associated membrane proteins. It is an object of the invention to provide proteins having homology to the vesicle associated protein, VAP-33, designated herein as PRO983.

44. PRO1057

Proteases are enzymatic proteins which are involved in a large number of very important biological